

AMENDMENT TO THE CLAIMS

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**Claim 1 (amended):** A method of ~~designing or selecting~~ identifying a compound which modulates binding of a natural ligand to ~~binds to a molecule of~~ the EGF receptor, ErbB3 or ErbB4, or which ~~family and~~ modulates ~~an activity mediated by the molecule~~ signal transduction via the EGF receptor, ErbB2, ErbB3 or ErbB4, which method comprises the steps of:

(A) assessing the stereochemical complementarity between the compound and a ~~topographic region of~~ the molecule, wherein the molecule comprises

(i) amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(ii) one or more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations;

(iii) amino acids present in the amino acid sequence of ~~a member of the EGF receptor family~~ ErbB2, ErbB3 or ErbB4, which form an equivalent three-dimensional structure to that of the receptor site defined by amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(B) obtaining a compound which possesses stereochemical complementarity to a ~~topographic region of~~ the molecule; and

(C) testing the compound for its ability to (i) modulate binding of a natural ligand to the EGF receptor, ErbB3 or ErbB4, or (ii) modulate ~~an activity mediated by the molecule~~ signal transduction via the EGF receptor, ErbB2, ErbB3 or ErbB4.

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Claims 2-5~~3~~ (canceled).

**Claim 54 (amended):** A The method according to claim 1, wherein the testing in step (C) is carried out *in vitro*.

**Claim 55 (amended):** A The method according to claim 54, wherein the testing is performed by a high throughput assay.

**Claim 56 (amended):** A The method according to claim 1, wherein the testing in step (C) is carried out *in vivo*.

**Claim 57 (new):** The method of claim 1, in which step (C)(ii) involves testing the compound for the ability to modulate EGF receptor, ErbB2, ErbB3 or ErbB4 mediated cell proliferation.

**Claim 58 (new):** The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) is defined by amino acids 313-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

**Claim 59 (new):** The method of claim 1, wherein the amino acids in step (A)(iii) are present in the amino acid sequence of ErbB2, ErbB3 or ErbB4 and form an equivalent three dimensional structure to that of the region defined by amino acids 313-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

**Claim 60 (new):** The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) is defined by amino acids 1-475 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

**Claim 61 (new):** The method of claim 1, wherein the amino acids in step (A)(iii) are present in the amino acid sequence of ErbB2, ErbB3 or ErbB4 and form an equivalent three dimensional structure to that of the region defined by amino acids 1-475 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

**Claim 62 (new):** The method of claim 1 which further includes the step of modifying the compound such that the compound comprises structural regions able to make contact with amino acid residues at the surface of the molecule lining a groove region as depicted in Figure 7, Figure 8 or Figure 9.

**Claim 63 (new):** The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) are the amino acids that form the  $\beta$ -sheet of the L1 domain of the EGF receptor.

**Claim 64 (new):** The method of claim 1, wherein the amino acids in step (A)(iii) are present in the amino acid sequence of ErbB2, ErbB3 or ErbB4 and form an equivalent three dimensional structure to that of the  $\beta$ -sheet of the L1 domain of the EGF receptor.

**Claim 65 (new):** The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) are the amino acids that form the  $\beta$ -sheet of the L2 domain of the EGF receptor.

**Claim 66 (new):** The method of claim 1, wherein the amino acids in step (A)(iii) are present in the amino acid sequence of ErbB2, ErbB3 or ErbB4 and form an equivalent three dimensional structure to that of the  $\beta$ -sheet of the L2 domain of the EGF receptor.

**Claim 67 (new):** The method of claim 1 which further includes the step of modifying the compound to enhance binding to a lower face containing the second  $\beta$ -sheet of the L1 and/or L2 domains, wherein the structure of the face is characterized by a plurality of solvent-exposed hydrophobic residues.

**Claim 68 (new):** The method of claim 67, wherein the hydrophobic residues include:

- (i) Tyr64, Leu66, Tyr89, Tyr93; and/or
- (ii) Leu348, Phe380 and Phe412.

**Claim 69 (new):** The method of claim 1 in which the compound is identified from test compounds in a database.

**Claim 70 (new):** The method of claim 1, which further includes the step of selecting a compound that increases signal transduction via the EGF receptor, ErbB2, ErbB3 or ErbB4.

**Claim 71 (new):** The method of claim 1, which further includes the step of selecting a compound that decreases signal transduction via the EGF receptor, ErbB2, ErbB3 or ErbB4.

**Claim 72 (new):** The method of claim 1, which further includes the step of selecting a compound that inhibits or prevents the binding of a natural ligand to the EGF receptor, ErbB3 or ErbB4.

**Claim 73 (new):** A method of identifying a compound which binds to a molecule of the EGF receptor family selected from the group consisting of the EGF receptor, ErbB2, ErbB3 and ErbB4, which method comprises the steps of:

(A) assessing the stereochemical complementarity between the compound and the molecule, wherein the molecule comprises

(i) amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(ii) one or more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations; or

(iii) amino acids present in the amino acid sequence of ErbB2, ErbB3 or ErbB4, which form an equivalent three-dimensional structure to that of the receptor site defined by amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(B) obtaining one or more compounds which possesses stereochemical complementarity to the molecule; and

(C) selecting a compound that has a  $K_d$  or  $K_i$  of less than  $10^{-6}$  for a molecule of the EGF receptor family selected from the group consisting of the EGF receptor, ErbB2, ErbB3 and ErbB4.

**Claim 74 (new):** A method as claimed in claim 73, wherein  $K_d$  is less than  $10^{-8}M$ .

**Claim 75 (new):** The method of claim 73, wherein  $K_i$  is less than  $10^{-8}M$ .